RCPA

The Royal College of Pathologists of Australasia

Extension of Scope of Practice in Molecular Genetics (NPAAC Supervision Certification Modules)

MICROBIOLOGY

TABLE OF CONTENTS

GLOSSARY

CPDP	RCPA Continuing Professional Development Program
(F)RCPA	(Fellow of the) Royal College of Pathologists of Australasia
IANZ	International Accreditation New Zealand
MDT	Multi-disciplinary team
NATA	National Association of Testing Authorities
NPAAC	National Pathology Accreditation Advisory Council
PPD	Personal Professional Development
RCPAQAP	RCPA Quality Assurance Programs Pty Ltd
SOP	Standard Operating Procedure
WHS	Workplace Health and Safety

SECTION 1

INTRODUCTION

The Royal College of Pathologists of Australasia (the College) offers a number of certification modules for Fellows of the Royal College of Pathologists of Australasia who have completed Fellowship in the discipline of Microbiology.

The modules do NOT apply to current microbiology practice in molecular diagnostics and Sanger sequencing, which are integral to the existing training, experience and responsibilities of clinical microbiologists. All clinical microbiologists will continue to be able to supervise this testing.

The development of the modules has been required to satisfy the recent NPAAC requirements (http://health.gov.au/internet/main/publishing.nsf/Content/health-npaac-docs-supervision.htm), particularly as applicable to testing involving diagnostic genomics (both human and microbial).

To adequately medically supervise a Whole Genome Sequencing (WGS) service, clinical microbiologists need to have adequate and detailed knowledge of the wet and dry lab aspects of the technology and bioinformatics analysis. It is recognised that this knowledge may not be the same as the hands-on experience of the scientist in WGS laboratory, however, supervising pathologists should be familiar with the limitations and strengths of the methodology, the ethical considerations of data use and reporting and the clinical relevance for assessing appropriate requesting and reporting.

It is anticipated that in the next few years, WGS will expand beyond specialised and reference laboratories. These modules are designed to provide all microbiologists with the opportunity to participate in accordance with NPAAC requirements.

GENERAL AIMS OF THE TRAINING PROGAM

The genetics/ genomics certification modules build on discipline-specific Fellowship training. As well as gaining additional competencies in genetics/ genomics relevant to microbiology, candidates are expected to extend further their skills in management, research, scholarship, as well as the professional qualities they have been developing during their pre- and post-Fellowship years and will continue to develop during their professional life.

This Handbook outlines requirements for the Microbiology Certification Modules. It is based on a common approach for Fellows in all pathology disciplines to develop/ demonstrate the minimum professional competencies required for safe clinical service provision of genetic/ genomic testing. As such, the certification modules and associated competency standards outlined within this handbook have shared features with the modules outlined in the equivalent handbooks for other disciplines.

The purpose of the modules outlined in this Handbook is to offer Fellows the opportunity to gain certification of expertise for a graduated range of genetic/ genomic testing categories specifically for clinical applications within their pathology discipline.

Completion of one or more modules would result in extension of scope of practice within Microbiology to the limits defined for each module. The scope of practice would not extend into other discipline areas – for example, investigation of intellectual disability or prenatal diagnostic testing.

An essential part of sub-specialty genetics/ genomics training is for practitioners to gain sufficient understanding of the breadth of the field; are aware of the limits of their own knowledge and appreciate when it is in the best interests of patients to refer onto, or formally consult with genetic pathologists or other appropriately credentialed colleagues

The certification modules build on discipline specific Fellowship training. Candidates are expected to further develop the skills in management, research, scholarship, and professional qualities they have been developing during their pre- and post-Fellowship years and will continue to develop during their professional life.

Please note: For candidates who currently have a scope of practice for Microbiology who wish to receive certification, can do by completing either Module 1 or Module 1 and 2. It will be assumed that those who have completed Module 1 will have sufficient knowledge and competency to complete Module 2. There will be no opportunity to complete Module 2 without completing Module 1.

Pathogen genomics refers to the use whole genome sequencing (WGS) technologies to obtain read data that can be analysed to enlighten various clinical and public health scenarios. WGS within microbiology pertains to all pathogens (e.g. bacteria, viruses, fungi and parasites) and can be performed from the isolate or directly from sample.

The goal of targeted sequencing can be considered broadly in 2 groups: those that pertain to a single pathogen and those projects that examine relationships between multiple numbers of the same pathogen of either specific public health interest or within hospitals. Examples of these two categories include high-resolution identification and characterisation of microbial pathogens; inferring drug resistance from whole genome sequence; relating individual cases to an outbreak of infectious disease and establishing the association between an outbreak and an environmental reservoir.

In contrast, non-targeted sequencing or metagenomics examines for the presence of pathogen(s) or the relative composition of different microbial populations within a specific niche (microbiome). The diagnostic utility of these applications is likely to increase in the future.

To address adequately the wide range of professional competencies required to supervise these activities, it is proposed that post-graduate training and assessment is delivered in two modules (with a third module to be considered in the future directed at non-targeted sequencing). The modules are a practical response to the gradient of technical and complexity within pathogen genomics, as well the differing practical skill sets required.

SECTION 2

LEARNING OUTCOMES AND RECOMMENDED TRAINING ACTIVITIES

Module 1 – Pathogen identification and characterisation using genome data.

Examples of clinical applications include –

- Identification of an isolate
- Inference of drug resistance from whole genome sequence (pathogen) only
- Inference of virulence determinants
- Inference of multi-locus sequence type

It is anticipated that this module will be progressively incorporated into the microbiology fellowship curriculum. In time, the need for this module to be offered as a specific post-fellowship training module will disappear. Meanwhile, there was general agreement that this module should be available as a post-fellowship option for microbiologists seeking to take responsibility for the pathology tests in this category.

Methodologies covered

Massive parallel sequencing using amplicon-based and/or capture-based assays.

General considerations

- This builds on a sound understanding of Sanger and the next-generation sequencing and analysis.
- No specific guidance pertaining to quality issues, validation and requirements of supervision of massive parallel sequencing pertaining to microbial sequencing has been agreed so far, however, these indicators are discussed in *Requirements for human medical genome testing utilising massively parallel sequencing technologies, National Pathology Accreditation Advisory Council, 2017*.

Wet lab considerations

- knowledge of technical performance, limitations and quality issues associated with different library preparation and sequencing techniques
- Knowledge of technical performance, limitations and quality metrics associated with different sequencing technologies
- appropriate specimen types and associated collection methods
- genomic DNA/RNA extraction method(s)
- nucleic acid quantity and quality indicators
- the role of positive, negative controls and reference stains
- trouble-shooting failed quality indicators
- characteristics of the specific factors pertaining to pathogen (e.g. RNA vs. DNA, gram positive vs. gram negative) and the design of sequencing experiments

Dry lab considerations/ Analysis considerations

- Knowledge of relevant bioinformatics issues including reference selection, capacity and limitations of alignment tools, variant callers used for variable determination (e.g. resistance or virulence genes).
- Knowledge of sequencing data and meta-data structure, data security/privacy regulations
- Understanding of available databases used for identification and characterisation of different pathogens, their limitations and processes of maintaining their content currency
- Understanding of cloud based secondary and tertiary analysis systems

Post-Analytic Considerations

- Ability to evaluate accuracy of WGS platforms and bioinformatics pipelines
- Ability to evaluate accuracy and precision of WGS results as well as their analytical and diagnostic sensitivity and specificity
- Ability to provide clinically appropriate advice regarding contents of genomic reports including diagnostic implications.
- Involvement and ability to communicate in multidisciplinary meetings with pathologists and other referring specialists.

Professional Competency

- **Log book** (generated reports of at least 50 isolates representing at least 5 different pathogens (i.e. not the same species) attained from more than 5 runs).
- **Case-based discussions** (It is anticipated that a different number of anomalies requiring troubleshooting will be encountered within the minimum requirement and it is recommended that potential problems are discussed)
- **Supervisor sign-off**
    - With sign-off indicating:
        - the principles of the method(s) are understood
        - working knowledge of instrument processes and maintenance requirements
        - successful generation of results at a quality level sufficient for reporting
        - strong understanding of QC procedures for the method, including internal and external QA
        - working knowledge of method anomalies and associated trouble-shooting

Module 2 – Pathogen genomics for the determination of relationships between isolates / generation of a phylogeny.

Examples of typical clinical applications include –

- relating individual cases to an outbreak of public health importance
- relating individual cases to an outbreak within a hospital
- investigation of the most likely transmission pathways within the outbreak
- to establish the association between the outbreak and a specific vehicle (e.g. environment or food source)

Similar to Module 1, it is anticipated that this module will be progressively incorporated into the microbiology fellowship curriculum. Meanwhile, there was general agreement that this module should be available as a post-fellowship option for microbiologists seeking to take responsibility for the pathology tests in this category.

General considerations

- This builds on a sound understanding of Core module 1
- Core module 2 can only be undertaken after or in conjunction with core module 1
- No specific guidance pertaining to quality issues, validation and requirements of supervision of massive parallel sequencing pertaining to microbial sequencing exist however, these indicators are discussed in *Requirements for human medical genome testing utilising massively parallel sequencing technologies, National Pathology Accreditation Advisory Council, 2017*.

Wet lab considerations

- General practical skills understanding of nucleic acid preparation method(s), library preparation and quality indicators as per core module 1.

Dry lab considerations

- Knowledge of technical performance, limitations and quality issues associated with different sequencing technologies as per core module 1.

Analysis considerations

- Knowledge of relevant bioinformatics as per module 1.
- Knowledge of limitation and strengths of different typing schemes using WGS data (e.g. in-silico MLST vs. cgMLST vs. wgMLST vs SNP-based similarity assessment)
- Knowledge of the effects of recombination and methods / and need to mask such events.
- Knowledge of the strengths and limitations of different tree building algorithms, software programs and visualisation tools
- Working knowledge and ability to use open-source software for genome similarity assessment, tree generation and genomic data visualisation

Post-Analytic Considerations

- Ability to provide clinically appropriate advice regarding contents of genomic reports as per core module 1.

Professional Competency

- **Log book** (generated reports of at least 3 phylogenies (trees) based on a minimum of 10 newly generated sequenced isolates (i.e. not downloaded from public available repositories)
- **Case-based discussions** *(Aimed at pathogen specific analysis exploring the limitations of various tree-building methods and interpretation)*
- **Supervisor sign-off**
    - With sign-off indicating:
        - That principles of all method(s) are understood including an adequate understanding of principals set out in core module 1.
        - Working knowledge of the intricacies of phylogenetic analysis.
        - Working knowledge and ability of open source software.

Module 3 – Microbiome

This module is currently on hold in it development. It is anticipated that this module will cover metagenomics and specimen-based sequencing.

